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Assessment Of Main Strong Ion Difference In Renal Failure Patients

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Abstract

The renal failure patients have more risk for hypervolemia due to water and electrolyte imbalance. Hypervolemia is caused by fluid retention which also occurs in congestive cardiac failure, liver failure, high blood pressure and too much infusion of intravenous fluids. The dialysis treatment for renal failure patients will remove the excess fluid and the non-protein nitrogenous substances that help to regulate the water and electrolyte balance. The renal failure patients develop metabolic acidosis. According to Stewart's acid base balance theory, metabolic acid base disturbances are due to the changes in strong ion difference but this concept is not routinely applied because their calculation is difficult and not all the ions are routinely measured. Some of the previous studies have shown that the apparent strong ion difference can be well predicted by the simplified main strong ion difference that includes only the sodium and chloride which are the major contributors to the apparent strong ion difference (SID). In this current research study, 126 renal failure patient cases are included. 4 groups using serum urea values and an another 4 groups using creatinine values are formed. The main strong ion difference is calculated for all the cases and the study concludes that it is lowered in all these patients irrespective of the different higher urea and creatinine levels but the comparison between different groups are statistically significant.

Keywords: Strong ion difference, sodium, chloride, urea, Creatinine.

Introduction

Azotemia is a medical condition characterized by abnormally high levels of urea, creatinine and other nitrogen rich compounds in the blood. The ratio between blood urea nitrogen (BUN) and Creatinine is a calculated parameter useful in determining the type of azotemia but this ratio alone does not provide an accurate differential diagnosis of pre -renal, renal and post renal causes.[1,2] Hypervolemia is caused by fluid retention that can occur in renal failure, congestive cardiac failure, liver failure, high blood pressure and intravenous infusion of too much fluids.

The kidneys play an important role in water, electrolyte and acid base balance. The patients with chronic kidney disease have more risk for hypervolemia due to water and electrolyte imbalance. The metabolic acidosis will be seen in renal failure patients. The dialysis treatment for renal failure patients will help to remove the excess fluid and the non-protein nitrogenous substances. This will help to regulate the water and electrolyte balance.[3,4]

The acid base disturbances are analysed using various approaches like physiological approach using bicarbonate, standard base excess approach and Stewart's physicochemical approach. By applying basic physicochemical laws, such as the law of mass action, law of conservation of mass and the law of electrical neutrality Stewart gave detailed explanation for the causation of metabolic acid base disturbances which are due to the changes in the independent variables namely strong ion difference and total concentration of non-volatile weak acids.[5,6,7]

Strong ions have complete dissociation in solution but weak acids only partially dissociate so, both dissociated form (anionic component A^-) and un-dissociated form (HA) are present in the solution. The **apparent strong ion difference (SID_a)** denotes the difference between sum of strong cations and anions and the normal value is **42 mEq/L.**[8] This is balanced by the effective strong ion difference (buffer base) to preserve electrical neutrality.[8,9,10]

The calculation of apparent strong ion difference includes cations like sodium, potassium, ionized calcium and magnesium and anions like chloride and lactate. If lactate is not measured then it will be included under strong ion gap which denotes the unmeasured ions. A commonly accepted reference range for strong ion difference is lacking in the literature. The concept of strong ion difference is not routinely clinically applied because their calculation is difficult and not all the ions are routinely measured. Some of the previous studies have shown that the apparent strong ion difference can be well predicted by the simplified main strong ion difference that includes only the sodium and chloride which are the major contributors to the apparent strong ion difference (SID).[11,12,13] The aim of the current research study is to assess the level of main strong ion difference in various groups of renal failure patients and to graphically analyse their relationship with parameters like urea, creatinine and serum osmolality.

MATERIALS AND METHODS:

The difference between sum of the strong cations and strong anions is called **apparent strong ion difference (SIDa)**. Buffer base **($[HCO_3^-] + [A^-]$)** is numerically the same as **effective strong ion difference (SID_e)**. [7,9,10]

SIDa = [sum of the strong cations] - [sum of the strong anions]

SIDe = $[HCO_3^-] + [A^-]$

$[A^-]$ or $[A^-$ tot$]$ **:** denotes the total concentration of dissociated non-volatile weak acids namely albumin (Alb) and phosphate (Pi).

Strong ion Gap (SIG):

SIG = SIDa - SIDe

{SIDe = $HCO_3^- + A^-$tot}

Strong ion gap = SIDa - HCO_3^- - A^-tot

HCO_3 = SIDe - A^- tot

HCO_3 = SIDa - A^- tot - SIG

If SIG is zero, then SIDe and SIDa are equal. [7,9,10]

Calculation of NRH^+ (Non-Respiratory hydrogen ion concentration):

The calculated hydrogen ion concentration equivalent of standard bicarbonate represents the 'non-respiratory hydrogen ion concentration' $[NRH^+]$. [9,10]

NRH^+ = 960 / Std HCO_3

SIDa - A^- tot - SIG = {960 / NRH^+} X HCO_3/Std HCO_3

The Stewarts parameter and the non-respiratory hydrogen ion concentration are related using the above relationship derived by Rajini Samuel. **Strong ion difference** is **inversely proportional** to the non-respiratory hydrogen ion concentration but the **total concentration of dissociated weak acids** (A^- or A^-_{tot}) and **Strong ion gap (SIG)** are **directly proportional** to the non-respiratory hydrogen ion concentration. [10]

This research study is a **retrospective study** done in the Department of Biochemistry at **Government kilpauk Medical College Hospital**, Chennai. A total of **126 renal cases** are included in this study and their estimated urea, creatinine and electrolyte values are noted. Based on **serum creatinine** values they are divided into **four groups (1.8 ≤ 4.0, >4.0≤8.0, >8.0≤13.0 and >13.0 mg/dl)**. Similarly based on **serum urea** values, **four groups** are formed **(42 ≤ 70, >70≤100, >100≤150 and >150 mg/dl)**. The **main strong ion difference (mSID)** which includes only the sodium and chloride is calculated for all the 126

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cases. From the previous research study, the **normal reference** value of the main strong ion difference is taken (which is **between 34** and **38 mEq/L**). It was mentioned that the main strong ion difference value less than 34 mEq/L predicted metabolic acidosis and a value more than 38 predicted metabolic alkalosis.[12]

Blood urea = 2.14 x BUN

Blood urea nitrogen (BUN) values are calculated by dividing the blood urea level by 2.14 and the ratio between BUN and serum creatinine is calculated.[1] Serum osmolality is usually calculated using the serum sodium, glucose, urea and ethanol. Many formulas are available to calculate it. The calculation can be simplified by using **sodium** and **urea** (or **BUN**) values or using sodium values alone. In this current study, we have used the values of serum sodium and BUN to calculate the serum osmolality.[14]

Serum Osmolality = 2 x Serum Sodium + BUN/2.8

RESULTS:

The **main strong ion difference (mSID)** is calculated using the serum sodium and chloride levels in each group and their **mean** and **standard deviation** is calculated (shown in **table 1**). **One Way ANOVA analysis statistical tool** is applied to compare the main strong ion difference values in four different groups based on serum urea and creatinine values which is found to be statistically significant (clearly shown in **table 1**). The various parameters like urea, creatinine, serum osmolality and main strong ion difference are graphically analysed and shown in the **figures 1 to 8**.

TABLE 1: main Strong Ion Difference (mSID) for the various Groups of Renal patients

Parameter	Group I	Group II	Group III	Group IV
Groups based on Creatinine mg/dl	1.8 ≤ 4.0	>4.0≤8.0	>8.0≤13.0	>13.0
Number of Cases	38	41	38	9
mSID Mean ± Std Dev	**21.82** ± **3.52**	**21.61** ± **4.19**	**19.45** ± **2.25**	**18.22** ± **3.90**
One Way ANOVA Analysis for groups based on Creatinine Values: The f-ratio value is 5.40. The p-value is .0016. The result is significant at p < .01.				
Groups based on Urea mg/dl	42 ≤ 70	>70≤100	>100≤150	>150
Number of Cases	36	37	42	11
mSID	**21.72** ± **3.56**	**21.70** ± **4.38**	**19.57** ± **2.32**	**19.18** ± **4.00**

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Mean ± Std Dev				
One Way ANOVA Analysis for groups based on Urea Values: The f-ratio value is 4.11. The p-value is .0081. The result is significant at $p < .01$.				

FIGURE 1: X: Axis serum Urea VS Y: Axis serum Creatinine

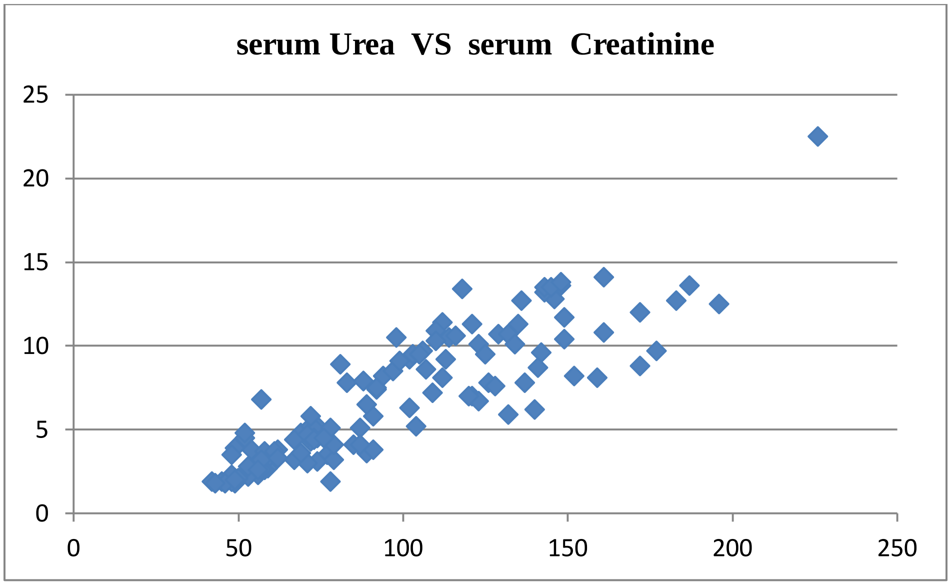

FIGURE 2: X: Axis main SID VS Y: Axis serum Urea

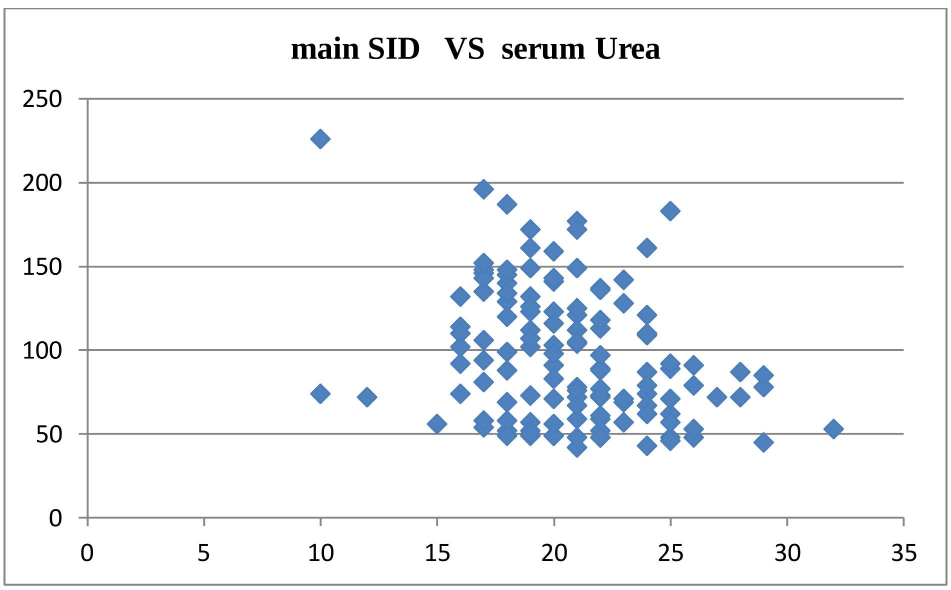

FIGURE 3: X: Axis main SID VS Y: Axis serum Creatinine

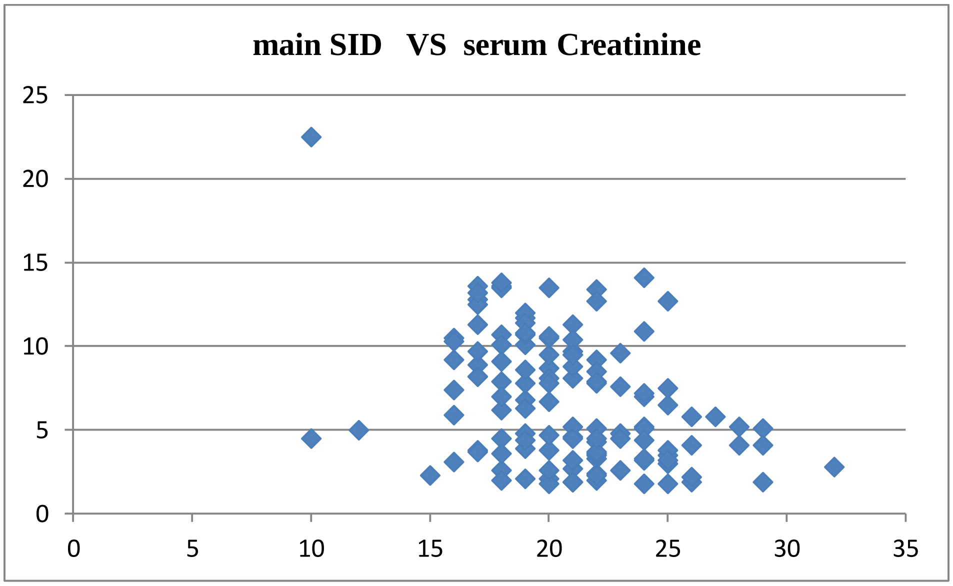

FIGURE 4: X: Axis main SID VS Y: Axis BUN/Creatinine Ratio

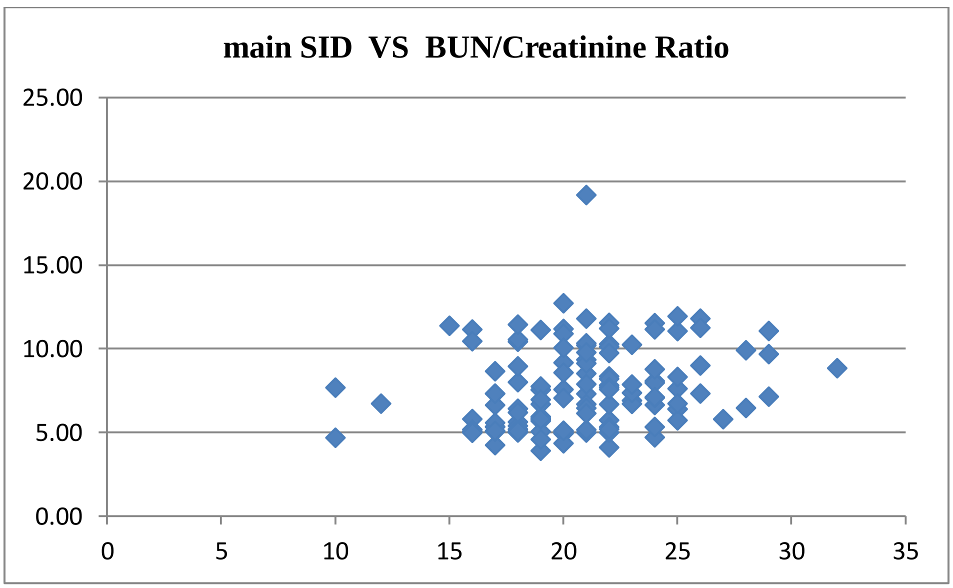

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FIGURE 5: X: Axis main SID VS Y: Axis serum Sodium

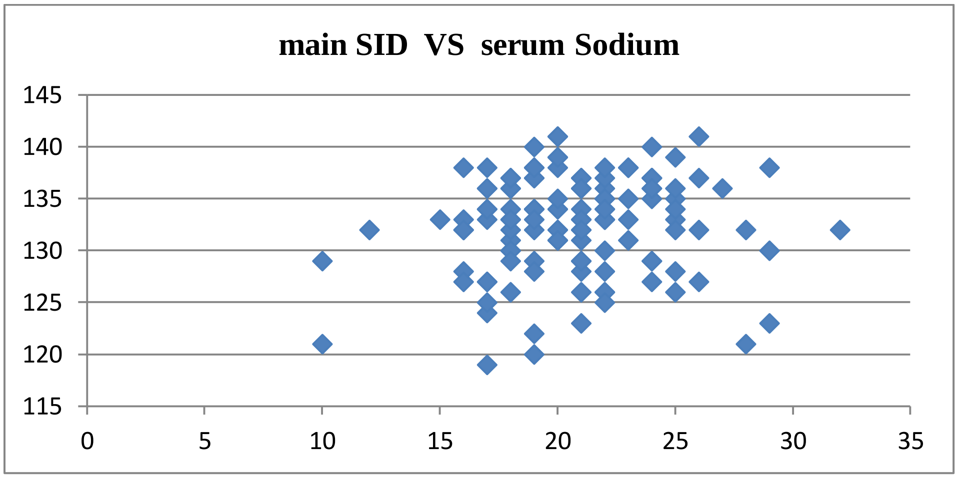

FIGURE 6: X: Axis main SID VS Y: Axis serum Chloride

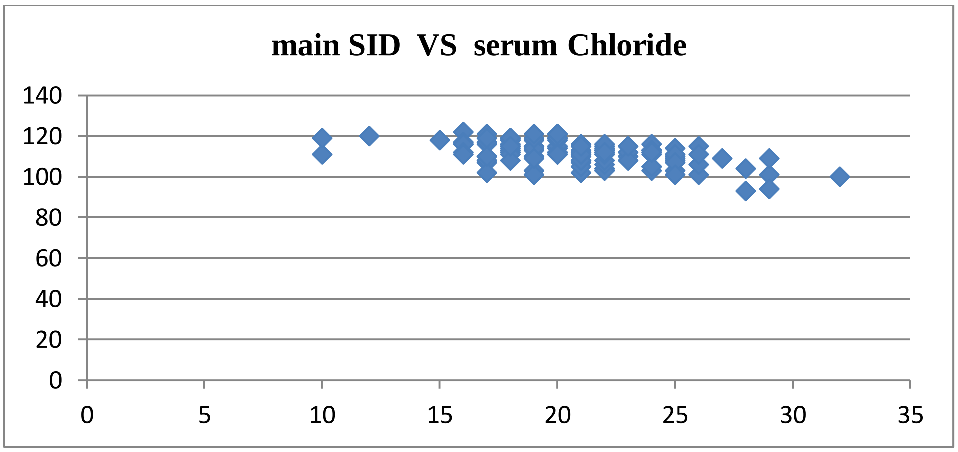

FIGURE 7: X: Axis main SID VS Y: Axis serum Osmolality

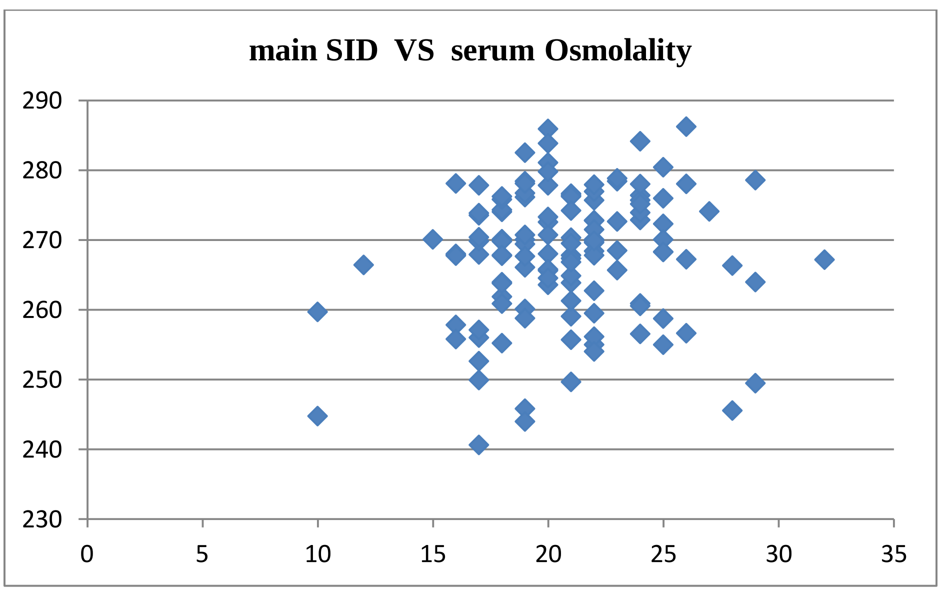

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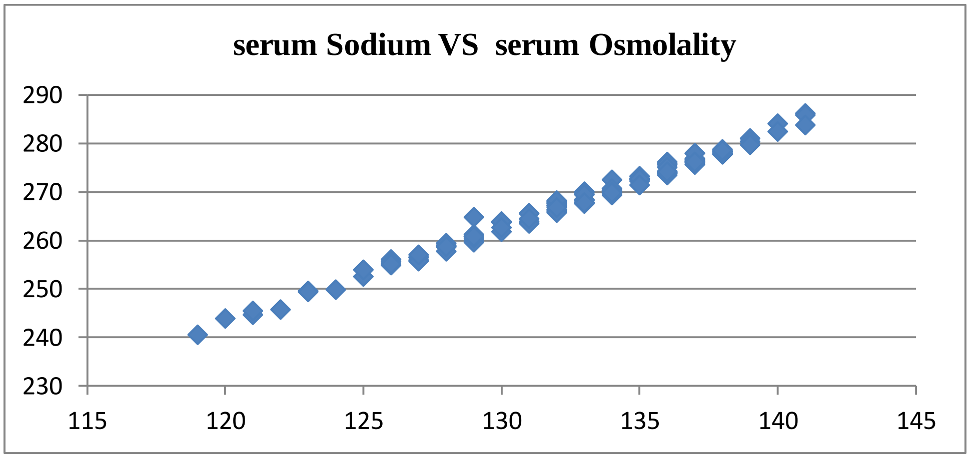
FIGURE 8: X: Axis Serum Sodium VS Y: Axis serum Osmolality



DISCUSSION:

The strong ion difference effect has a powerful **electrochemical effect** on **water dissociation**. The sodium and chloride are the major contributors of the strong ion difference. The water is **amphoteric** because it can behave **both** as an **acid** and a **base**. The ionic product of water is the product between the concentration of hydrogen and hydroxyl ions which is a constant at a given temperature. The product of hydrogen ion [H^+] concentration and the hydroxyl ion [OH^-] concentration is a constant. If the hydrogen ion concentration increases the hydroxyl ion concentration decreases and vice versa to maintain the constant ionic product of water. The water dissociation is very little so, the hydrogen ion concentration in the body fluids are in nanomoles/L.[10,15]

The main **strong ion difference** value is **decreased** if the concentration of negative anion (**chloride**) is **increased** or the concentration of positive cation (**sodium**) is **decreased**. Then the **water** behaves like an acid and dissociates more **hydrogen ions (positive charge)** to maintain electrical neutrality. So whenever **SID** is **decreased** it results in **acidosis**. Similarly the main **strong ion difference** value is **increased** if the concentration of negative anion (**chloride**) is **decreased** or the concentration of positive cation (**sodium**) is **increased**. Then the **water** behaves like a base and dissociates more **hydroxyl ions (negative charge)** to maintain electrical neutrality. So whenever **SID** is **increased** it results in **alkalosis**. Dehydration and over-hydration changes the strong ion difference by concentrating or diluting the concentration of these ions respectively.[10,15]

Strong ion difference is **inversely proportional** but the **total concentration of dissociated weak acids** is **directly proportional** to the **non-respiratory hydrogen ion** concentration.[10] Higher non-respiratory hydrogen ion concentration will result in metabolic acidosis and lower non-respiratory hydrogen ion concentration will result in metabolic alkalosis.[9,10]

From the **figure 1**, it is very clear that as the creatinine concentration increases the urea also increases but not proportionately because urea, the end product of protein metabolism is a variable parameter. The relation between main strong ion difference with urea, creatinine and BUN/creatinine ratio is shown in the **figures 2,3** and **4** respectively. From these graphs, it is very clear that decreased main strong ion difference is seen for the different values of urea and creatinine and not necessarily for higher values alone. The relation between main strong ion difference with sodium, chloride and serum osmolality (calculated using sodium and BUN) is shown in the **figures 5,6** and **7** respectively. The **main strong ion difference** value is **reduced irrespective** of the **individual values** of **serum sodium** and **chloride** concentration. Decreased values of main strong ion difference are seen with the following different conditions like normal sodium (with increased chloride), lowered sodium,(normal or increased chloride), normal chloride (with reduced sodium) and increased chloride (with normal or decreased sodium). The serum osmolality mainly

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depends on the serum sodium concentration and it is directly related to it, which is clearly depicted in the **figure 8**. In this current study, the **main strong ion difference (mSID)** is lowered in renal failure patients irrespective of the different higher urea and creatinine levels but the reduction compared between the different groups based on urea and creatinine value is statistically significant. This simple and easily calculated main strong ion difference will serve as an indicator for metabolic acid base disturbances which may help in assessing the severity of the condition.

CONCLUSION:

The main strong ion difference calculated using sodium and chloride is reduced in all the renal failure patients which will contribute to metabolic acidosis. The study concludes that the assessment of the main strong ion difference plays a significant role in the understanding of the causative mechanism and management of these patients.

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